

Amendments to the Specification:

Please replace paragraph [0015] beginning at page 4, line 6, with the following:

--[0015] Figure 2 shows a BlastP alignment of *Pyrococcus furiosus* polymerase (Pfu) (query 1; SEQ ID NOS:1 and 2) against *Pyrococcus sp* GB-D polymerase (Deep Vent®) (subject 1; SEQ ID NOS:3 and 4). Consensus sequences = SEQ ID NOS:5 and 6.--

Please replace paragraph [0017] beginning at page 4, line 13, with the following:

--[0017] Figure 4 shows the sequences of the parental Dut proteins (E. coli dut = SEQ ID NO:7; AAD = SEQ ID NO:8) and the BLASTP alignment of the parent sequences. E. coli dut = SEQ ID NO:9; AAD = SEQ ID NO:10; Consensus peptides = SEQ ID NOS:11-15.--

Please replace paragraph [0018] beginning at page 4, line 15, with the following:

--[0018] Figure 5 shows the degeneracies at the positions that differ in the parental Dut proteins (SEQ ID NOS:7 and 8). 5A.: Aligned parental sequence showing all possible codons in order of frequency of use by *E. coli*. 5B: Consensus sequence is derived by finding codons that will encode both sequences with a minimal number of degeneracies (SEQ ID NOS:16 and 17). Codons frequently used by *E. coli* are preferred. 5C: Nucleic acid degeneracies that incorporate amino acid sequences not similar (BLOSUM 62 number is <0) to either parental amino acid sequence are removed; in this example the nucleic acid encoding the thermal stable protein sequence, AAD is used instead (SEQ ID NOS:18 and 19). These are indicated in bold. The sequence of the thermal stable enzyme is also used in deciding to retain the one gap and eliminate the 2 cases where terminating codons could be incorporated in the sequence.--

Please replace paragraph [0019] beginning at page 4, line 25, with the following:

--[0019] Figure 6 shows the priming and restriction sites (bold) that were added to the ends of the sequence (SEQ ID NO:20). In two cases, codon usage was changed to add restriction sites (underlined and in italics). The amino acids encoded by the sequence are indicated below the codons (SEQ ID NO:21).--

Please replace paragraph [0020] beginning at page 4, line 28, with the following:

--[0020] Figure 7 shows the minimal encoding oligonucleotide sequence to be synthesized to assemble the Dut hybrid library (SEQ ID NO:20). The DNA sequence was converted to single letter nucleotide code using standard designations and oligonucleotide sequences were selected (below in bold). Selections were made such that minimal degeneracies exist where primers were expected to anneal to each other during assembly. In one stretch of sequence there was no region where reasonably sized annealable oligonucleotide sequences could be selected. In this example, the ClaI site (underlined) inserted in the previous step is used to assemble a full-length protein-encoding library from 2 restriction fragments.--

Please replace paragraph [0021] beginning at page 5, line 6, with the following:

--[0021] Figure 8 shows the minimal encoding sequence (SEQ ID NO:22) used to generate oligonucleotides encoding a Pfu/ Deep Vent® Hybrid DNA polymerase (SEQ ID NO:23) as explained in example 2. The degenerate nucleotides are in parenthesis. The amino acid sequences that differ between the parent proteins (the "mismatches") are indicated. Non-parental amino acids are indicated in bold. Examples mentioned in the text are numbered.--

Please replace paragraph [0024] beginning at page 5, line 19, with the following:

--[0024] Figure 11 shows a comparison of the sequences of parent and hybrid polymerase proteins (SEQ ID NOS:24-37).--

Please replace paragraph [0097] beginning at page 23, line 17, with the following:

--[0097] Expression control sequences that are suitable for use in a particular host cell are often obtained by cloning a gene that is expressed in that cell. Commonly used prokaryotic control sequences, which are defined herein to include promoters for transcription initiation, optionally with an operator, along with ribosome binding site sequences, include such commonly used promoters as the beta-lactamase (penicillinase) and lactose (*lac*) promoter systems (Change *et al.*, *Nature* (1977) 198: 1056), the tryptophan (*trp*) promoter system (Goeddel *et al.*, *Nucleic Acids Res.* (1980) 8: 4057), the *tac* promoter (DeBoer, *et al.*, *Proc. Natl. Acad. Sci. U.S.A.* (1983) 80:21-25); and the lambda-derived P_L promoter and N-gene ribosome binding site (Shimatake *et al.*, *Nature* (1981) 292: 128). The particular promoter system is not critical to the invention, any available promoter that functions in prokaryotes can be used. Standard bacterial expression vectors include plasmids such as pBR322-based plasmids, *e.g.*, pBLUESCRIPT™, pSKF, pET23D, λ-phage derived vectors, and fusion expression systems such as GST and LacZ. Epitope tags can also be added to recombinant proteins to provide convenient methods of isolation, *e.g.*, c-myc, HA-tag, 6-His (SEQ ID NO:38) tag, maltose binding protein, VSV-G tag, anti-DYKDDDDK (SEQ ID NO:39) tag, or any such tag, a large number of which are well known to those of skill in the art.--

Please replace paragraph [0107] beginning at page 26, line 5, with the following:

--[0107] To facilitate purification of the hybrid polypeptides of the invention, the nucleic acids that encode the fusion polypeptides can also include a coding sequence for an epitope or "tag" for which an affinity binding reagent is available. Examples of suitable epitopes include the myc and V-5 reporter genes; expression vectors useful for recombinant production of fusion polypeptides having these epitopes are commercially available (*e.g.*, Invitrogen (Carlsbad CA) vectors pcDNA3.1/Myc-His and pcDNA3.1/V5-His are suitable for expression in mammalian cells). Additional expression vectors suitable for attaching a tag to the fusion proteins of the invention, and corresponding detection systems are known to those of skill in the art, and several are commercially available (*e.g.*, FLAG" (Kodak, Rochester NY). Another example of a suitable tag is a polyhistidine sequence, which is capable of binding to metal chelate affinity ligands. Typically, six adjacent histidines (SEQ ID NO:38) are used, although one can use more or less than six. Suitable metal chelate affinity ligands that can serve as the binding moiety for a polyhistidine tag include nitrilo-tri-acetic acid (NTA) (Hochuli, E. (1990) "Purification of recombinant proteins with metal chelating adsorbents" In Genetic Engineering: Principles and Methods, J.K. Setlow, Ed., Plenum Press, NY; commercially available from Qiagen (Santa Clarita, CA)).--

Please replace paragraph [0123] beginning at page 29, line 29, with the following:

--[0123] The final primers chosen in this example are indicated below. Assembly would occur as follows: Fwd1 primer is annealed to RevA primer. In separate tubes, Fwd2 is annealed to RevB, Fwd3 to RevC, Fwd4 to RevD, and Fwd5 is annealed to Rev5. The products of the five annealing reactions are primer extended with a DNA dependent DNA polymerase with proof reading activity, typically *E. coli* DNA polymerase I Klenow fragment, or the thermal stable Phusion polymerase (MJ Research, Inc.). If Phusion polymerase is used, it is possible to thermally cycle the primer extension reaction. The products of the Fwd1/RevA reaction are

annealed to the products of the Fwd/2/RevB reaction and extension is repeated. Similarly, the products of the Fwd4/RevD reaction are annealed to the Fwd5/RevE reaction and extended. Finally, the Fwd1/RevA/Fwd2/RevB products are annealed to the Fwd3/RevC products and extended.

Oligonucleotides:

Fwd 1 (SEQ ID NO:40): 5'-TTGGTACCAA GCTTCATATG A-3'

Fwd 2 (SEQ ID NO:41): 5'-CC GCTGCCGASC TATGCGACCY CTCACAGCKC
AGGCCTGGAT CTGCGTGCG-3'

Fwd 3 (SEQ ID NO:42): 5'-TTCCG ACCGGTCTGA TCMTTSAWAT TSCGGAWGGT
TMTGMGGSGC AGRTGCKGCC GCGTAGCGGC CTGG-3'

Fwd 4 (SEQ ID NO:43): 5'-TTTTGATCGA TRSCGATTAT CRGGGCSAAS TGAWGRTTAK
CSTGGTGAAC CKGGGCMASG AWGAAKTRY GATTAGCSG GGCGAACGTA
TTGCGCAG-3'

Fwd 5 (SEQ ID NO:44): 5'-CGTGGCGAA GGCGGCTTTG GCTCTASCGG CASAMAGTAA
TGAGGATCCG AATTCTT-3'

Rev A (SEQ ID NO:45): 5'-
GGTCGCATAGSTCGGCAGCGWAAWTCTTKGSCATGASGCRGACGCWKAATTTTCA
SAWYAAAYTTTKYTCATATGAAGCTTGGTACCAA-3'

Rev B (SEQ ID NO:46): 5'-
GATCAGACCGGTCGGAAYCAGCRYCSTWTCAMMCGGCKYAAKTTYCASCOSWTYST
YAAKGSMCGCACGCAGATCCAGGCCTG-3'

Rev C (SEQ ID NO:47): 5'-

TTTTATCGATCRKGCCCRSCGCGTTCAGCASCRTAWGCCMTKTTTCCAGSCCAGGC
CGCTACGCGGC-3'

Rev D (SEQ ID NO:48): 5'-

TAGAGCCAAAGCCGCCTTCGCCACGMTSGGTCTGAGAAAMWTCTTCCACCWSAWY
AAMTTCCRCCYGCWSCACCGGCRCAAWAAYCAKCTGCGCAATACGTTTCGCCC-3'

Rev E (SEQ ID NO:49): 5'-AAGAATTCGGATCCTCATTACT-3'--

Please replace paragraph [0140] beginning at page 35, line 25, with the following:

--[0140] To measure exonuclease activity, a 45 base long primer with the following sequence was synthesized: 5'-FAM-TTTTTTGAGGTGTGTCCTACACAGCGGAGTGTAGGA CACACCTCT* 3' (SEQ ID NO:50), wherein T*= is an amino-link dT with the quencher, DAB (dabcyl) attached. The sequence forms a 16 base pair stem loop structure with a T:T* mismatch at the quencher-labeled base. The 5' unbase-paired poly T sequence keeps FAM (6 carboxy-fluorescein) in close proximity to the quenching dye so the FAM, if excited, it will not fluoresce.--

Please insert the accompanying paper copy of the Sequence Listing, page numbers 1 to 87, at the end of the application.